

## Pharmacy Policy Bulletin

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**Title:** Heart Failure Agents

**Policy #:** Rx.01.174

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***Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.***

***This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.***

***Members are advised to use participating pharmacies in order to receive the highest level of benefits.***

### **▶ Intent:**

The intent of this policy is to communicate the medical necessity criteria for **Corlanor® (ivabradine) and Entresto® (sacubitril/ valsartan)** as provided under the member's prescription drug benefit.

### **▶ Description:**

Heart failure affects approximately 5.1 million Americans. While survival after a diagnosis of heart failure has improved, it is still about 50% at 5 years after diagnosis. In patients with symptomatic heart failure and left ventricular ejection fraction (LVEF)  $\leq$  40%, current guidelines recommend angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB), beta blockers, diuretics and aldosterone antagonists as standard of care. With the exception of diuretics, these classes of medications decrease mortality from heart failure with reduced EF. Diuretics provide symptomatic relief, however the effects of diuretics on morbidity and mortality are not known.

Ivabradine reduces spontaneous pacemaker activity at the cardiac sinus node by blocking the hyperpolarization-activated cyclic nucleotide-gated (HCN) channel to selectively inhibit  $I_f$ -current, thus reducing the heart rate. Ventricular repolarization and myocardial contractility are not affected. Increased heart rate is an ineffective compensatory mechanism and is recognized as an independent risk factor in heart failure.

Corlanor® (ivabradine) is indicated to reduce the risk of hospitalization for worsening heart failure in patients with stable, symptomatic chronic heart failure with left ventricular ejection fraction  $\leq$  35%, who are in sinus rhythm with resting heart rate  $\geq$  70 beats per minute and either are on maximally tolerated doses of beta blockers or have a contraindication to beta-blocker use.

Sacubitril inhibits neprilysin via its active metabolite, LBQ657. Valsartan inhibits the effects of angiotensin (AT) II by selectively blocking the AT1 receptor.

Entresto® (sacubitril/ valsartan) is indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction. Entresto® is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other ARB.

▸ **Policy:**

Corlanor® (ivabradine) is approved when ONE of the following is met:

1. Diagnosis of stable, symptomatic chronic heart failure and ALL of the following:
  - a. LVEF  $\leq$  35%; and
  - b. Sinus rhythm with resting heart rate  $\geq$  70 beats per minute; and
  - c. Patient is clinically stable for at least 4 weeks on an optimized and stable clinical regimen which includes:
    - i. Maximally tolerated doses of beta blockers or inability to tolerate beta blockers; and
    - ii. ACE inhibitors or ARBs or inability to tolerate ACE inhibitor or ARB
- OR
2. Diagnosis of inappropriate sinus tachycardia and BOTH of the following
  - a. Inadequate response or inability to tolerate BOTH of the following
    - i. One beta-blocker; and
    - ii. One calcium channel blocker
- AND
- b. Prescribed or recommended by a cardiologist

Entresto® (sacubitril/ valsartan) is approved when ALL of the following are met:

1. Member is 18 years of age or older; and
2. Diagnosis of chronic heart failure with NYHA functional class II-IV; and
3. Ejection fraction less than 35%; and
4. Concurrent administration of or inability to tolerate beta blockers

▸ **Black Box Warning:**

Entresto® (sacubitril/ valsartan): When pregnancy is detected, discontinue ENTRESTO as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus.

▸ **Guidelines:**

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

## **BENEFIT APPLICATION**


Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

▸ **References:**

1. Borer JS, Bohm M, Ford I, et al. Efficacy and safety of ivabradine in patients with severe chronic systolic heart failure (from the SHIFT study). Am J Cardiol. 2014;113:497-503.

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3. Entresto (sacubitril/ valsartan) [package insert]. East Hanover, NJ. Novartis Pharmaceuticals Corporation. August 2015. Available from: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=000dc81d-ab91-450c-8eae-8eb74e72296f&type=display>. Accessed November 9, 2018.
4. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics-2013 update: a report from the American Heart Association. *Circulation*. 2013. Doi: 10.1161/CIR.0b013e31828124ad. Available from: <http://circ.ahajournals.org/content/127/1/e6.full.pdf+html>. Accessed November 12, 2018.
5. Ivabradine. Micromedex. Available from: <http://www.micromedexsolutions.com>. Accessed November 21, 2018
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7. Swedberg K, Komajda M, Bohm M, et al. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study. *Lancet*. 2010;376 (9744):875-85.
8. Yancy CW, Jessup M, Bozkurk B, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2013. Doi: 10.1016/j.jacc.2013.05.020. Available from: <http://circ.ahajournals.org/content/128/16/e240.full.pdf+html>. Accessed November 12, 2018.
9. Yancy CW, Jessup M, Bozkurk B, et al. ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update to the 2013 ACC/AHA Guidelines for the Management of Heart Failure. *Circulation*. 2016. DOI: 10.1161/CIR.0000000000000435. Available from: <http://circ.ahajournals.org/content/circulationaha/early/2016/05/18/CIR.0000000000000435.full.pdf>. Accessed November 12, 2018.
10. Cappato R, Castelvécchio S, Ricci C, et. al. Clinical Efficacy of Ivabradine in Patients with Inappropriate Sinus Tachycardia. *Journal of the American College of Cardiology*. Vol. 60, No 15, 2012. October 9, 2012: 1323-9
11. Olshansky B, Sullivan R. Inappropriate Sinus Tachycardia. *Journal of the American College of Cardiology*. Vol. 61, No 8, 2013. February 26, 2013:793-801.
12. Sheldon RS, Grubb BP, Olshansky B, et. al. 2015 Heart Rhythm Society Expert Consensus Statement on the Diagnosis and Treatment of Postural Tachycardia Syndrome, Inappropriate Sinus Tachycardia, and Vasovagal Syncope. Available at: <https://www.hrsonline.org/Policy-Payment/Clinical-Guidelines-Documents/2015-HRS-Document-on-POTS-IST-VVS>. Accessed 12/11/2018.

**Applicable Drugs:**

 Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Corlanor®	ivabradine
Entresto®	sacubitril/ valsartan

**➤ Cross References:**

N/A

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<b>Policy Version Number:</b>	5.00
<b>P&amp;T Approval Date:</b>	October 11, 2018
<b>Policy Effective Date:</b>	January 1, 2019
<b>Next Required Review Date:</b>	October 11, 2019

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The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.